NEONATAL VIROME IN CULTURE-NEGATIVE SEPSIS AND SYSTEMIC INFLAMMATION IN PRETERM NEONATES

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Background: Culture-negative sepsis is often used to describe neonates who are deemed symptomatic and treated with antibiotics, but blood cultures are negative. It is unclear if culture-negative sepsis is related to viruses, fungi or other microbes that cannot be cultured, or inflammation. The viral microbiome (or, virome) is a dynamic community of eukaryotic DNA and RNA viruses, bacteriophages, and endogenous retroviruses that are poorly characterized. The virome has been shown to play an essential role in immune system development, immunomodulation, and adult inflammatory bowel disease. However, there is limited data on the neonatal virome and its role in 'culture-negative sepsis.' We hypothesize that the neonatal virome, and its perturbation, plays an important etiological role in culture-negative sepsis and mediates systemic inflammation.

Materials/Methods: In a prospective nested study, we will enroll preterm neonates born at <37 weeks' gestation undergoing sepsis evaluation. We will compare the composition and diversity of the virome from 20 neonates with culture-positive sepsis, 20 neonates with culture-negative sepsis, and 20 asymptomatic, healthy preterm neonates. Virome evaluation will be performed from blood, stool, nasopharyngeal and skin swabs at the Center for Metagenomics and Microbiome Research laboratory.

Results: We are in the process of enrolling patients and have enrolled 42 neonates who underwent sepsis evaluations. Our hypothesis stems from a prior study that confirmed the presence of a circulating blood microbiome in healthy neonates. We earlier reported significant decrease in alpha diversity (Shannon Diversity Index (SDI)) and operational taxonomic units (OTUs) of the blood microbiome in neonates with central line associated bloodstream infection (CLABSI) vs. uninfected neonates. When neonates with CLABSI were compared to those without, the blood microbiome showed a significant decrease of Acinetobacter ($p=0.023$) and Faecalibacterium ($p=0.048$) at the level of the genus but no differences at the phylum level.

Conclusions: Prior research has confirmed the presence of the blood microbiome in uninfected preterm infants and the feasibility of its evaluation. Our current research aims to determine the diversity and composition of the virome at the time of sepsis evaluation, as well as to determine its association with systemic inflammation and neonatal outcomes. This research could underpin the pathophysiology of culture-negative sepsis in relation to the virome and systemic inflammation.

Images / Graph / Table

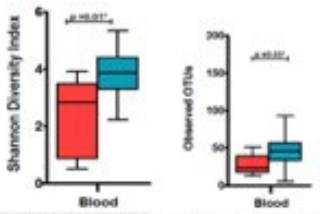

Figure 1a: Significant decrease in Shannon diversity index and observed OTUs in the blood microbiome of patients with CLABSI (infected) compared to those who did not (uninfected)

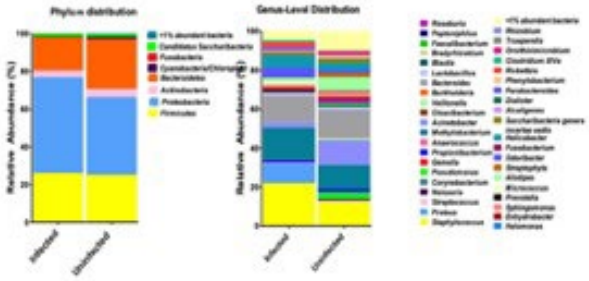

Figure 1b: Summary of taxonomic distribution at the phylum and genus levels in the blood of preterm infants. Infected infants show an increase in Proteobacteria and a decrease in Bacteroidetes (not statistically significant). At the genus level, a significant decrease of *Acinetobacter* (p=0.023) and *Faecalibacterium* (p=0.048) was observed.